Letters to the Editor

Innov Clin Neurosci. 2017;14(9–10):3

AN OPEN-LABEL PROPHYLAXIS STUDY OF LITHIUM PLUS EXTENDED-RELEASE CARBAMAZEPINE (ERC-CBZ) COMBINATION FOR RAPID CYCLING BIPOLAR DISORDER

Dear Editor:

Rapid cycling bipolar disorder involves the occurrence of four or more episodes of mania and/or major depression within a year and is characterized by a treatment-refractory course with high morbidity. As rapid cycling patients often do not respond well to lithium monotherapy, mood stabilizer combinations have been recommended for long-term treatment.[1] Positive findings have been reported in rapid cycling patients treated with lithium combined with mood stabilizers such as carbamazepine as compared to monotherapy.[2,3] Extended-release carbamazepine (ERC-CBZ) has important advantages over immediate-release carbamazepine, including reduced fluctuations in serum carbamazepine levels and a decrease in CNS side effects.[4] Our objective was to evaluate the safety and efficacy of lithium plus ERC-CBZ for prophylaxis in patients with rapid cycling bipolar disorder.

We recruited 16 patients with DSM-IV defined bipolar disorder with a history of rapid cycling in the past 12 months and on stable lithium therapy for six months or longer. In the preliminary study phase, patients received ERC-CBZ at starting doses ranging from 100mg to 200mg twice daily depending on clinical presentation and titrated up to a maximum dose of 1,600mg/day over a two-week period. All psychotropics other than lithium, ERC-CBZ, and benzodiazepines were then tapered over a two-week period. Patients stabilized on lithium and ERC-CBZ then entered a six-month open-label phase and completed biweekly visits. The primary efficacy measure was time to relapse as estimated using the Kaplan-Meier method. Relapse was defined by (a) a need for additional pharmacotherapy for affective symptoms, (b) hospitalization for an affective episode, and (c) increase of more than 50 percent in Hamilton Depression Rating Scale (HAM-D) and Young Mania Rating Scale (YMRS) scores from baseline. Secondary efficacy measures included changes in symptom severity on the HAM-D, YMRS, and Clinical Global Impression (CGI) scales.

Of the 16 patients who enrolled in the study, 56 percent were men ranging in age from 28 to 59 years (M=39.4). At baseline, the mean HAM-D score was 10.6 (SE=1.7), and the mean YMRS score was 9.6 (SE=2.4). Twelve patients entered the open-label phase. Six patients experienced a relapse with the median time to relapse estimated as 144 days. One patient was lost to follow-up at 14 days, one patient dropped out of the study for SAE at 61 days, and four patients completed the study. The 100-day relapse rate was 27 percent (95% CI: 10–63%). Using repeated measures and a mixed-effects model, HAM-D total score, YMRS total score, and CGI severity and improvement scores did not change significantly between visits 6 and 18 (p>0.1).

Rapid cycling bipolar disorder is highly resistant to treatment, although research evidence regarding optimal treatment for rapid cycling patients has been limited.[5] The findings from this study suggest that lithium combined with ERC-CBZ might be safe and effective for prophylaxis in patients with rapid cycling bipolar disorder, although the small sample size and high lost-to-follow-up rate are clear limitations. Randomized controlled trials are needed to validate these preliminary findings.

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With regard,

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Keywords: carbamazepine, lithium, rapid cycling, bipolar disorder

Funding/financial disclosures: This work was supported by an investigator-initiated grant from Shire Pharmaceuticals. ICNS